THE AMERICAN
JOURNAL OF PHARMACY

VOL. 107 JUNE, 1935 No. 6

EDITORIAL

THE AVAILABILITY OF POISONS

ONCE upon a time we thought of the detective only as a slant-eyed sleuth in gum shoes, slick on the gun-draw, slicker still with changing his wardrobe and whiskers, and always ready with a lightning flick of his coat lapel to broadcast his badge and business.

But latterly, the detection of crime has grown to be a serious business—and men trained in precision—the finger-print expert, the microscope man, the chemist, the physicist—all are part of the great dragnet that covers the country for its criminal catch.

No matter how we may react to the New Deal, whether we are Rooseveltian or just old-fashioned Americans, the administration's Mr. Hoover and his G men must claim our respect and admiration for their first-rate accomplishments and for the far-reaching policies of their special department.

If the influence of the professors and their applied sciences are responsible in part for the improvement in this special work of the Department of Justice, then we hail not only Hoover but all the professors as well.

For not only is the department making crime more difficult and less attractive, because of its obvious success at apprehending the perpetrators, but its wise policy of propaganda, its nation-wide warning that crime does not pay, must be deterrent to many who might otherwise err.

With broadcasts, magazine articles, special bulletins, newspaper editorials and similar agencies—the inevitability of punishment for crime, the relentlessness of the law, the practical demonstrations of the operation of justice in the recent public enemy prosecutions, all of these facts are blatantly brought to general notice.

And this is a splendid means of prevention. It is an antidote to the poison virus needled into the minds of our youngsters by mawkish gangster pictures on the screen, by sentimentalized piffle printed in our daily papers, and by the gunman glorifying gags in our muck-raking magazines.

We call attention however to an oversight in connection with a minor phase of this campaign of education.

It has to do with poisons—and it is a two-fold criticism.

In the first place, the actual naming of toxic materials in the context of articles dealing with such is greatly to be deplored. One article, which may or may not be part of this anti-crime propaganda, appears in that alleged he-man magazine, *Esquire,* and mentions in no uncertain terms the specific names of the poisons discussed, thus affording the reader a sort of an extra-mural education in the fine art of poisoning.

The second criticism has to do with the unfortunate availability of poisons to those who mean to use them criminally. The most insidious toxic weapons, more gruesome than the gun, may be bought as readily as ribbon at the counter, by anyone who wants them. The arsenic, cyanide and nicotine insecticides are sold as glibly as sugar—by the grocer, the florist, and the hardware man.

And, more than likely, their use is often else than insecticidal.

The pharmacist must register his sales of every poison, but poison more wicked than the bite of a mad dog's tooth may be bought elsewhere without a whit of ceremony.

Consider that concentrate of nicotine sulfate, sold for rose-tree spraying, and containing in the vile little vial enough poison to end the days of half a dozen adults.

And although the advent of the modern analyst has stolen the subtlety from the poisoner's repertoire, there is still enough incentive, still enough opportunity for intelligent scoundrels to try their toxic tricks.

Poisons are altogether too easy to get—too easy to use and abuse.

IVOR GRIFFITH.

ORIGINAL ARTICLES

NEWER CONCEPTS OF PUBLIC HEALTH*

By George W. McCoy, M. D.

Director of "The National Institute of Health"

ONE of the entrancing things about medicine, especially preventive medicine, is the never ending series of changes, all let us hope in the direction of improvement and of advancement. The orthodox of one decade has become the obsolete of the next—indeed, often much less than a decade serves to change the classification. Medicine often is accused of being ultra-conservative but if we view it in contrast with, let us say, the law, or with social and economic practices and customs, I think we shall have to concede that medicine loses nothing by the comparison. Perhaps one reason why those of us in the medical field have the reputation of being slow to change is the fact that we encounter so many visionary, so many alluring, and so many illusive projects that we have become somewhat canny.

We are constantly amazed at the readiness with which those without practical experience in medicine, particularly in the field of public health, find ready solutions for problems that have baffled the profession for many years. These ready solutions are not always the proposals of the untrained layman. Occasionally they originate with someone having a very good background of training and experience in some other branch of science. If medicine is becoming more cautious, it is also becoming less gullible. Once we have established the bedrock of truth it does not take long to adapt our practice to it. In the last couple of decades there have been so many advances in the administrative field of preventive medicine that it is a little difficult to choose exactly the example best suited for our needs, but I will give two illustrations:

During the period of active service of officers still on duty in the Public Health Service it was customary, when dealing with a ship infected with yellow fever, to painstakingly "disinfect" the ballast even though this ballast might be nothing but rock. Then along came the work of Reed and his associates which showed that ballast had nothing

*Commencement Address, June 5, 1935, Philadelphia College of Pharmacy and Science.

to do with the transmission of this infection, but that a certain type of mosquito had everything to do with it. Almost overnight practice changed, and, instead of thinking of the perfectly harmless ballast, attention was directed to the terribly harmful mosquito!

My second example is one that perhaps is more familiar to most of us. Up to about fifteen years ago nearly everywhere it was the routine custom to fumigate the quarters occupied by the sick after recovery from almost any one of the common infectious diseases. I suppose this custom was the evidence of survival of the fetish that diseases were something occult and connected with a given locality. Then came a courageous health officer with vision, who decided to discontinue fumigation after contagious disease and, to his gratification but not to his surprise, he found that the health of his community was in no wise jeopardized by deliberately ignoring what up to that time had been handed down by all authority as the proper procedure. Administrative health officers rapidly began to give up the time-honored fumigation until now, for practically all of the ordinary infectious diseases, the so-called terminal fumigation has become obsolete.

In relation to purely "hygienic" measures we are becoming more definite. We have long stressed the importance of good food, sunshine, and fresh air. We are beginning to realize that the "good" food must be specifically good. To take the single example of scurvy; the "good" food must contain the vitamin which is effective in preventing scurvy. Sunshine we know is specifically protective against rickets, but if the sunshine is not available, or to be had only in inadequate amounts, the cunning of the chemist has provided a substitute. Fresh air serves chiefly to dilute and carry away deleterious gases and infecting agents.

I do not expect to present anything original, but I will give you several examples, largely from the work of the Public Health Service, illustrating what I consider to be notable advances of comparatively recent years.

Pellagra

Perhaps not even this name is familiar to you, but I assure you that in the southeastern part of the country, all the way from Virginia to Texas, the term is well understood and the disease is all too commonly encountered. While you are not especially concerned in the purely medical phases of the subject, I may say that pellagra is char-

acterized by a rash that may affect any part of the body but which appears usually on the hands, feet, forearms, neck and face. The rash is usually accompanied by a stomatitis—a highly inflamed, reddened mucous membrane of the mouth—digestive disturbance, weakness, loss of weight; if unchecked, the disease goes on to mental deterioration. Twenty years ago our ideas of the cause, and therefore of the prevention and cure, of this disease were most uncertain and unsatisfactory. At about that time the majority of orthodox students of the subject inclined to the view that in pellagra we had a member of the large group of contagious, or infectious diseases, a view still occasionally expressed. At about that time, Doctor Goldberger, who came from Pennsylvania, proceeded to make a careful study of the problem. Pellagra was at that time a disease notably prevalent in institutions for the insane and in orphanages. The first thing to strike this young scientist was the fact that the disease regularly spared the attendant and nursing staffs of these institutions. The thought came to him that this fact was scarcely compatible with an infectious disease, since if some contagion were being spread, that is, if the disease were communicable from person to person, surely the physicians, nurses, ward maids, and others in close association with the victims would not escape, although escape they did with mathematical regularity. Then, too, it was recognized that, running through the story of pellagra for a century, there was the suspicion that in some way it was associated with diet, but the only tangible theory in this direction was that foods derived from corn, or corn products, preferably somewhat the worse for age and wear, were responsible. The clear visioned research worker to whom I have referred proceeded in a very direct manner to determine how this baffling disease originated. First, with the consent and co-operation of a broad-visioned executive of a Southern State, volunteers in a prison camp were selected and by suitable adjustments of diet it was found possible to cause the disease in a great majority of these volunteers though their companions, living in the same general environment, continued to escape. This one strong bit of evidence established that pellagra was related to diet. Second, a reverse experiment was performed. Institutions in which the disease was prevalent were asked to make certain supplements to what was considered an inadequate diet, and in these institutions as soon as the dietary changes were inaugurated pellagra was entirely prevented or vanished if it had already appeared. There are many further de-

tails in connection with the solution of this problem but what I have said illustrates the simple, direct, early attack which gave the foundation for our knowledge as to the cause and prevention of this disease. The later work has shown rather definitely that the disease is due to lack in the diet of a very specific element which has been classified as one of the growing group of vitamins. You may ask why we still have pellagra in the South and in other parts of the world, for indeed it is still all too prevalent. The answer to this is that, at least for this country, the dietary habits of large groups of the population are exceedingly difficult to change, so difficult that it would appear that a new generation must arise with a clear understanding of the significance of these discoveries before we shall have seen the last of pellagra. Another factor is that the disease is one almost exclusively of individuals of a poor economic status and from this point of view the solution is bound up with changes in the social and economic system, which in the very nature of things are very slow in developing.

Amebic Dysentery

Data in older sections of this country in which records long have been kept as to sickness and death show that only two or three generations ago dysentery was an exceedingly common cause of illness and was one of the main causes of death. Of course, those records all date back to a period before we knew anything definite about how infectious diseases were spread—in other words, before the germ theory had been evolved and when we were still in ignorance of the cause of what we now speak of as an infectious disease. I want to discuss briefly just one of the types of dysentery. The old designation "dysentery" included the type which we call "amebic," and doubtless many other types. Two things which the most distinguished authorities stated with respect to amebic dysentery were: (1) The disease never was epidemic and, furthermore, it never could be. (2) It was a disease confined almost exclusively to warm climates—in other words, a tropical disease, although I must point out that there was in the medical lore of the day plenty of evidence to show that the disease might be regarded as much more cosmopolitan in its distribution than its designation "tropical" connoted. Coupled with these statements was almost complete ignorance of the way in which the disease was communicated from person to person or from some other source to the human victim. The most commonly held view was that the healthy

carriers of the organism in one stage of its life cycle were the most probable source of infection with amebic dysentery. Then came one of the unforeseen and, as I view it, practically unpredictable tragedies of public health. In the summer of 1933 cases of amebic dysentery began to appear all over this country. In the early part of the outbreak physicians generally were not prepared to recognize the nature of the disease even when suggestive symptoms developed in their patients. They were not thinking of amebic dysentery, or thought of it only as a tropical disease. The disease was called by almost any name other than the correct one. This epidemic reached a total of something over a thousand reported cases with about 100 deaths. Of course, I realize that this number of cases and deaths in a population of 120 millions is not of special public health significance, but the public health significance of the episode comes from the fact that we could have, and did have, an epidemic of a disease hitherto regarded as never occurring in epidemic form in a civilian population. The evidence pointed overwhelmingly to one city as a distributing point for the infection, and soon the same evidence pointed very specifically to certain hotels in that city. Perhaps less certainly, but still in very convincing fashion, all indications showed that a local contamination of the water supply of these hotels was responsible for the outbreak.

Spotted Fever

There are several kinds of spotted fever but we are concerned now with only one of them—the so-called Rocky Mountain spotted fever, which up to about five years ago was regarded as occurring exclusively in a rather restricted area in the northwestern states, notably Wyoming, Montana, and Idaho. All authorities laid stress on the fact that the disease occurred only in scattered areas in the States mentioned, and that it was not known to occur anywhere else in the world. It varied greatly in prevalence, and especially in fatality, in the different areas in the infected regions. Research studies carried on in the early part of the present century had shown that the disease practically invariably was conveyed by a certain tick. A few reports had been published of a spotted fever-like condition in the East, but all of us felt that this latter condition must be something else because —did not all authority agree that Rocky Mountain spotted fever occurred only in the restricted region of the Northwest? Finally, about five years ago, by a combination of keen clinical observation and well-

designed laboratory experiments carried on by several of my associates, it became clear that we had spotted fever of the Rocky Mountain type in the East, and, what was equally surprising, when old evidence was reviewed it became clear that it had been with us a long time. It was found also that in the East the disease was caused by a tick but of a species different from that which transmitted the infection in the far West. So now in this period of only a few years physicians and health officers in the South Atlantic and Gulf States have learned to recognize that what had been considered hitherto exclusively a northwestern disease is moderately common in certain other parts of the country.

Typhus Fever

This is another member of the group of spotted fevers. Until a few years ago it was regarded as confined for the most part to Europe. Since then it has been recognized that typhus fever occurs very widely throughout the world. It has been known to occur sporadically in some of our large northern cities since early in the present century. The work of Doctor Brill in New York established this fact. A few years ago it was recognized that it occurred fairly extensively in some of our eastern seaboard cities south of New York. There was nothing particularly important about this since the disease, as we see it in this country, is self-limiting and has an exceedingly low death rate and shows no tendency to spread extensively, as it usually did abroad. The important thing lay in the discovery that this typhus which we have in the United States is not louse-borne, as is the case with European typhus, but that man is infected by the bite of the rat flea. What was perhaps even more important was the discovery that the rat was a natural host of typhus infection. From the facts stated came what is now the generally accepted view of the maintenance of typhus in the world. This view (and it has much to support it) considers typhus as prevalent and undetected among the rat populations, being transmitted between rats by their fleas. Occasionally it "slops over," so to speak, from the rat to man, giving us a case of human typhus. If it chances that the infected human being is the carrier of the common body louse and lives in a lousy population the stage is set for spread in epidemic form. To put it another way: We may say that *endemic* typhus is flea-borne and *epidemic* typhus is louse-borne, the ultimate source of infection in the first instance being the rat, and in the second instance the infected human being.

Virus Infections

I suppose one of the most striking of the relatively newer concepts of disease relates to what we speak of as the virus infections—measles, typhus, mumps, and several others. An easy definition for a virus infection would be that it is a disease brought about by germs as yet unrecognized and not yet cultivated. Though our knowledge regarding the germs causing these diseases is scanty we know much of their behavior and their effects on individuals and on the community. The St. Louis epidemic of encephalitis of 1933 is an example of what I have in mind. It was due to a type of infection not hitherto prevalent, or only lightly prevalent, in this country—possibly even in the world, since no exact counterpart appears to have been unearthed. We have learned a great deal about the virus causing this disease but I regret to say we have learned nothing that is likely to prove helpful in preventing a recurrence. Perhaps the most interesting feature about it is the fact that according to much evidence this infection is widely distributed throughout the country even though rarely has it resulted in an outbreak. In other words, it appears to exist in the form of a "latent" or "silent" infection.

Immunity

We are only beginning to suspect certain interesting relationships in the field of immunity to infectious disease. Is there a non-specific resistance? Certain facts suggest this. In a general way, it may be said that those who live in cities, particularly in the very crowded parts of cities, are less susceptible to at least certain of the infectious diseases than are those who dwell in rural communities. There is some evidence that what has been called the "experience" of the body with recognized, or even with unrecognized infections may promote resistance to other infections.

Some General Considerations

We are passing through a process of revision and adjustment in our public health handling of various problems. This is largely because of the uncertainty as to just what affords the greatest measure of protection to the community. Let us take leprosy for an example: We are really not much beyond the injunctions laid down by Moses in the Bible when he saw no better way of handling a leper than to exclude him from mingling with other members of the tribe.

From that day—indeed, perhaps from a period even earlier than Biblical times—the general attitude has been one of rigorous exclusion of the victim of leprosy from the remainder of society—either this or a complete ignoring of the potentialities for harm. We are just now beginning to reach a middle ground, with a relaxation of some of the rigors. Perhaps the biggest factor in bringing about this changed attitude on the part of the medical professions, and perhaps to some extent on the part of the general public, is the realization by health authorities that we have not made much progress in the handling of this disease, even by imposing most burdensome restrictions on the victims. Now we find it becoming popular to give the patient a considerable amount of liberty, and out-patient clinics are being tried as a substitute for segregation in institutions.

Curative medicine is becoming increasingly important in the field of public health. Proponents argue that if organized society is within its rights in endeavoring to prevent disease (and we all admit this) why is it not equally obligated to alleviate the burden if these efforts fail? This is readily conceded in the field of mental and infectious diseases but meets with much resistance when extended to medical practice in general, so we have had raised for us the question of "state medicine," though none of us knows just what we mean by the term and doubtless no two mean just the same thing. As a member of the medical profession, I fail to get excited about the subject. When the smoke of the fires of controversy has cleared we shall doubtless have a better system of caring for the sick than we now have, one that will distribute the burdens of illness so as not to wreck the financially unstable. Experiments under medical guidance are under way which justify the hope that we shall soon know the best system for carrying out the practice of curative medicine. It is most unlikely that the private practice of the medical art, including pharmacy, can survive, unchanged, in the midst of the social and economic developments that are going on so rapidly in this and other countries but I suspect that whatever alterations occur will come so gradually that we shall not be conscious of any violent disturbance of the system. Certain it is that we need a better mechanism for making available to more people the high grade of medical and surgical talent that the country affords.

In the field of therapeutics, change is ceaseless—let us hope that change is synonymous with progress. A good example of this is in

the treatment of tuberculosis which has changed within the last twenty years from the doctrine of forced feeding and fresh air to moderation in both of these, and most striking of all it has become largely a problem for the surgeon.

Comparatively recently the orthodox medical treatment for typhoid fever was an absolute milk diet continued sometimes over many weeks. This has been replaced by a saner prescription which permits of a generous diet and one free from the element of monotony inherent in the older practice.

There are certain diseases which, from the public health point of view, are still quite beyond our control. Our research has not enabled us to make any definite progress against them but has perhaps served to clear away some of the misunderstandings or to correct some of the errors. Influenza is an example. From a practical point of view we know no more about the disease than did our ancestors who from the dawn of history were afflicted by this periodically occurring scourge, a scourge which sweeps over the world every twenty-five or thirty years, the latest great invasion being in the latter period of the war and in the months following the end of the war. This was the first excursion of the infection since many new methods of study of disease had come into vogue. Scientists made renewed attacks all along the line, attacks which were vigorously and persistently carried on, but without successful outcome. There did come out of these studies the knowledge that the germ which we thought was responsible for this disease was in reality not related to it in any fashion.

Another example is to be found in infantile paralysis. Here we are substantially without any means of defense unless possibly the vaccines about which we have heard so much during the last year may prove to be beneficial. I do not wish to be unduly pessimistic about these vaccines, but I warn you that much more work must be done before we will know their field of usefulness, if any. The questions to be solved are substantially as follows: Are any of these vaccines really efficacious in man? If they are, for how long a period may immunity conferred be expected to last? Are they free from dangers which seem inherent in this class of therapeutic and prophylactic agents? If we answer all of these questions in favor of the vaccines there remain certain other considerations, as follows: Should these vaccines be recommended for general use at all times, as is the case with smallpox vaccine, or should we limit their application to seasons of special

risk, that is, when the disease threatens or is prevailing in a community? When we have answered all of these questions satisfactorily there would still be the question as to whether a vaccine prepared, let us say, with reference to an epidemic in New York will prove effective when tried in an epidemic in some other part of the country. All of the questions I have suggested must be solved by patient study. We would be deluding ourselves if we thought that a practicable vaccine for infantile paralysis is "just around the corner."

One of the most intriguing of the unsolved problems in relation to public health relates to the waxing and waning of epidemics. Why do they start, and why do they stop? Do they build up by passing from person to person, and terminate by the exhaustion of susceptible individuals? Is the immunity established by recognized and unrecognized forms of the infection a factor in bringing the scourge to an end? Do changes inherent in the infecting organism itself (possibly induced through influence of the host through which it passes) bring the epidemic to an end? We have little substantial information on any of these points. The solution remains for the research worker of the future.

In the field of what we generally call "Eugenics," perhaps more specifically indicated by the term "Race Betterment," progress is halting and slow chiefly because we do not know just what is right from the point of view of the future. Shall we allow the unfit to multiply and become burdens on society because defective stocks occasionally produce a genius, or because of the doctrine of the inherent right to produce offspring? The field is one beyond my special interest, but I confess that I find myself a disciple of the late Mr. Justice Holmes, who, when rendering a Supreme Court decision, announced: "Three generations of imbeciles are enough"—and, in support of this, said:

> "We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the State for these lesser sacrifices, often not felt to be such by those concerned, in order to prevent our being swamped with incompetence. It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind." (*The Advance of Science,* Watson Davis, 1934, p. 277.)

THE ESTIMATION OF ALKALOIDAL SALTS BY THE DIRECT TITRATION OF THEIR ACID RADICLES

Felice A. Rotondaro, Ph. D.*

IN 1885 Eugene Leger (1) called attention to the fact that alkaloidal salts are neutral towards phenolphthalein. He stated that "it is possible to estimate an acid volumetrically as easily when combined with certain alkaloids as when in the free state" and that "this may serve, within certain limits, to indicate the purity of a salt of the alkaloids". Several years later P. C. Plugge (2) made the volumetric estimation of the acid radicle in salts of alkaloids by using litmus as indicator and titrating directly with standard soda solution. He noted that in the titration of brucine, morphine and thebaine a red coloration appears before the end of the reaction when phenolphthalein is used as the indicator. He was aware that in solutions of alkaloidal salts (except those of the very feeble bases) the amount of free acid can usually be determined by titrating with litmus as indicator while the total acidity can be obtained by titrating to a phenolphthalein end point. L. Barthe (3) pointed out that the method is not applicable in the case of atropine or narcotine, but that the results are not affected by the presence of salts of the alkalis or alkaline earths.

A review of the various volumetric methods for the estimation of alkaloids was presented by Otto Linde (4) in two papers—dated respectively 1899 and 1900. He listed the indicators, their sensitiveness, and the solvents to be avoided with the use of each. He advised workers to avoid an excess of indicator, to have the solution as concentrated as possible, and to work at ordinary temperatures.

In 1909 Ernst Runne (5) made a series of titrations of alkaloidal salts and found that in alcoholic solutions morphine is slightly acid to Porrier's blue while quinine, cocaine and codeine are neutral. The following facts were soon recognized: phenolphthalein is not reddened by any of these four alkaloids in alcoholic solutions but in aqueous solutions codeine is markedly alkaline, morphine and cocaine alkaline to a lesser degree, and quinine is neutral; only quinine hydrochloride can be titrated accurately in either alcohol or water and with either of the two indicators; quinine sulfate, cocaine hydrochloride, and codeine phosphate can be titrated only in alcoholic or alcohol-water solutions with either indicator; morphine salts cannot be titrated accurately under any of the above conditions.

*The Zemmer Laboratory, Pittsburgh, Pennsylvania.

Recently, in 1933, M. B. Shvartzman (6) recommended the direct titration of alkaloidal salts with standard alkali and the use of phenolphthalein as indicator. The following year Schlemmer and Koch (7) reported good results from replacement titration employing alcoholic KOH after the addition of 90 per cent. ethyl alcohol and making use of either phenolphthalein or thymol blue as indicator. They also reported the titration of the basic (alkaloidal) group with alcoholic HCl after the addition of methyl acetate.

On the whole, a direct titration of alkaloidal salts has not been entirely satisfactory because of the different dissociation constants of the various members of the group in the different solvents. This makes it difficult to produce a color change sharply enough defined to give the reaction a quantitative significance. To overcome these difficulties, A. B. Lyons (8) suggested the use of chloroform to "withdraw the alkaloid from the aqueous solution as fast as it is set free by the alkali." By the use of neutral chloroform and with methyl red as indicator, he obtained satisfactory results for the salts of morphine, quinine and strychnine.

In accordance with Lyons' suggestion the writer undertook a series of experiments to find, if possible, "some other solvent that might be better . . . and another indicator . . . better suited for the titration".

A valuable suggestion for such a solvent was found in the work of George L. Schaeffer (9) on the solubilities of alkaloids in methyl alcohol. Schaeffer stated that the solubility of morphine, for instance, in 98-99 per cent. methyl alcohol is one gram of the alkaloid to fifteen grams of the alcohol—whereas it takes 200 g. of 80 per cent. alcohol to dissolve the same quantity of alkaloid at 25 degrees C. He also stated that, although morphine is said to be insoluble in benzene alone, a mixture of one part methyl alcohol with three parts benzene will produce a good solvent (1:40).

The extreme difficulty experienced in obtaining sharp end points in alcohol-water solvents is recognized. The decreasing solubility of alkaloids in alcohol with increasing amounts of water is also known. With these facts in mind the writer arrived at the conclusion that benzyl alcohol (phenyl methyl alcohol) might prove to be a satisfactory solvent. This was found to be true. All available literature has been carefully checked and no references have been found to indicate that anyone has employed benzyl alcohol as a solvent for alkaloids or that it has been used previously as a medium in the titration of acid radicles in alkaloidal salts.

While working out the details for a method of procedure in the titration it was learned that with some alkaloids, especially atropine, it is necessary to avoid the presence of water as much as possible. As to the choice of an indicator, it was found that phenolphthalein gives the most satisfactory results for two reasons: (a), it is not affected by the alkaloids dissolved in the benzyl alcohol—hence there is no shading of coloration due to them—and (b), the reaction is primarily one of neutralizing a strong acid by a strong base.

METHOD: Place 0.10 to 0.15 g. of the alkaloidal salt (accurately weighed) in a glass stoppered Ehrlenmeyer flask containing 40-50 ml. neutral benzyl alcohol. Then add a few drops of phenolphthalein indicator solution and run in approximately 90 per cent. of the quantity of 0.02 N KOH solution (carbonate free) calculated to neutralize the acid radicle of the salt. Place the stopper in the flask and shake thoroughly. When the pink coloration has disappeared continue the titration by adding successively small portions of alkali solution and shaking thoroughly after each addition. The emulsion which forms after the first additions of the alkali solutions breaks very readily as the neutral point is approached. The small globules which form as the emulsion begins to break are the first to show a pinkish tinge. At this stage the addition of a drop or two of the indicator helps the globules to coalesce (due to the alcohol in the phenolphthalein T. S.) and deepens the pink coloration in the supernatant aqueous layer. Shake the flask thoroughly and allow to stand for a few minutes. If, on adding another drop of indicator to the aqueous layer, the pink coloration is deepened the titration is considered completed. If the aqueous layer shows a decided reddish coloration, overtitration has taken place and the excess alkali must be titrated back by 0.02 N H_2SO_4 solution.

It has been found necessary to run a blank on the benzyl alcohol by adding 10-15 ml. of 0.02 N H_2SO_4 solution, shaking thoroughly, and titrating to an end point exactly as in the regular titration. Allow the two layers to separate completely and pour off as much of the supernatant aqueous layer as possible. Add the sample to the neutralized benzyl alcohol and proceed with the titration.

This titration method has been used by the writer since 1927 as a control method in the preparation of compressed and hypodermic tablets. In the case of compressed tablets a blank run on the diluents has been found to be desirable. The diluents of hypodermic tablets, however, seldom introduce an error greater than plus

or minus 0.20 per cent.—the approximate accuracy of the method. Consequently the preparation of the sample consists of powdering a representative number of tablets, weighing a portion of the powder calculated to yield from 0.10 to 0.15 g. of the salt, placing the powder in the flask containing the neutralized alcohol and titrating.

The following table shows same typical results obtained by titrating stock U. S. P. salts:

Sample	*No.*	*Taken*	*Found*	*Percentage*
Atropine Sulphate	1	0.1058	0.1045	98.77
	2	0.1235	0.1230	99.60
	3	0.1483	0.1487	100.27
	4	0.1155	0.1158	100.25
	5	0.0943	0.0937	99.36
Codeine Sulphate	1	0.1274	0.1269	99.53
	2	0.1055	0.1048	99.33
	3	0.1373	0.1375	100.14
Ephedrine Hydrochloride	1	0.1050	0.1043	99.33
(Not U. S. P.)	2	0.1120	0.1118	99.82
	3	0.0950	0.0951	100.10
	4	0.0840	0.0839	99.88
Ethylmorphine Hydrochloride	1	0.1035	0.1028	99.32
	2	0.1245	0.1247	100.16
	3	0.0945	0.0938	99.26
Morphine Sulphate	1	0.1153	0.1147	99.48
	2	0.1260	0.1250	99.20
	3	0.1020	0.1025	100.49
	4	0.1095	0.1100	100.49
Quinine Bisulphate	1	0.1137	0.1125	98.96
	2	0.0950	0.0954	100.42
	3	0.0985	0.0979	99.39
Quinine Sulphate	1	0.1015	0.1025	100.98
	2	0.1225	0.1230	100.41
	3	0.0993	0.0998	100.50
	4	0.1447	0.1450	100.20
Strychnine Nitrate	1	0.1030	0.1023	99.32
	2	0.1378	0.1380	100.14
Strychnine Sulphate	1	0.1175	0.1173	99.83
	2	0.1025	0.1030	100.48
	3	0.0963	0.0957	99.14

REFERENCES

(1) Leger, Eugene: "Phenolphthalein as an Indicator." *J. pharm. et chim.* (Ser. 5), **11**, 425-428 (1885).
(2) Plugge, P. C.: "Volumetric Estimation of Acids in Salts of the Alkaloids." *Arch. Pharm.* (Ser. 3), **25**, 45-59 (1887).
(3) Barthe, L.: "Volumetric Estimation of Alkaloids." *Compt. rend.*, **115**, 512-514 (1893).
(4) Linde, Otto: "The Volumetric Estimation of Alkaloids." *Arch. Pharm.*, **237**, 172-185, 392-408 (1899); **238**, 102-135 (1900).
(5) Runne, Ernst: "Titration of Alkaloidal Salts." *Apoth. Zeit.*, **24**, 662-663 (1909); **25**, 137 (1910).
(6) Shvartzman, M. B.: "On Direct Titration of Alkaloidal Salt With Standard Alkali and Phenolphthalein Indicator." *Farm. Zhur*, 229-231 (1933). (Original not seen.) *Chemical Abstracts*, **28**, 3524 (1934).
(7) Schlemmer, F., and Koch H.: "The Assay of Alkaloids by Replacement Titration." *Arch. Pharm.* (Ser. 3), **272**, 394 (1934).
(8) Lyons, A. B.: "Direct Titration of Acids in Alkaloidal Salts." *J. Am. Pharm. Assoc.*, **1**, 525-526 (1912).
(9) Schaeffer, G. L.: "Solvents for Alkaloids and Alkaloidal Salts." *Am. J. Pharm.*, **85**, 430-442 (1913).

Vitamin "A" and "D" Products

The Food and Drug Administration has received numerous inquiries about the proper labeling of products represented to contain vitamins A or D or both.

Many products compare their vitamin A and D potency with a stated volume of cod liver oil. If statements of this character are made, they should be literally true. For example, if the label of a medicine states "Each tablet equals one teaspoonful of cod liver oil in vitamins A and D potency," it should contain the same number of vitamin A and D units as would be contained in not less than 4 cc. (3.67 grams) of cod liver oil, of U. S. P. potency. In terms of the U. S. P. standard for cod liver oil which became official on January 1, 1935, this would require each tablet to contain not less than 2200 units of vitamin A and not less than 312 units of vitamin D.

Manufacturers should state vitamin A and D potencies in terms of the new U. S. P. units. Because differences in the clinical efficacy of vitamin D from different sources have been reported, it is desirable, and in many instances necessary in order to meet the requirements of the Federal Food and Drugs Act, to state the source of the vitamins A and D. For example, "From cod liver oil." All direct and implied claims comparing products of this sort with cod liver oil should be true in terms of the new standard for cod liver oil.

REPLACEMENT OF THE AMINO GROUP OF AROMATIC AMINES BY HYDROGEN*

By L. Chas. Raiford and Fred W. Oberst

GRIESS (1) showed that diazonium salts react with alcohol to give the corresponding aromatic hydrocarbons, and this was confirmed by Fischer and Fischer (2). Meanwhile, Wroblevsky (3) found that if the diazonium salt obtained from 2-amino-4-chlorotoluene is treated with alcohol the diazo complex is replaced by the ethoxy radical to give a mixed ether.

In later work Remsen and Orndorff (4) obtained a tolyl ethyl ether from each of the corresponding diazonium salts, with the largest yield from the ortho compound (5). The para compound alone gave toluene, also. Jackson and Moore (6) reported a 95 per cent. yield of *sym*-tribromobenzene obtained by this method from 2, 4, 6-tribromoaniline. In an extended study Cameron (7) reached the conclusion that replacement of the diazo complex by the alkoxy radical is the normal reaction, and that introduction of hydrogen is a modification induced by special conditions, notably the presence of "acid radicals" such as halogen and the nitro group. Mai (8) found that diazonium salts obtained from aniline, *p*-toluidine, benzidine and *α*-naphthylamine are decomposed by hypophosphorous acid to give 60 per cent. yields of the corresponding hydrocarbons. Amines containing ortho or "acidic" substituents were not tested.

The present work was done to test further the action of alcohol and hypophosphorous acid, respectively, on diazonium salts that contain "acidic" substituents.

Experimental Part

The amino compounds were purified until their physical constants agreed with those recorded in the literature.

In the first method the amine was dissolved in alcohol, the necessary amount of sulfuric acid added, and the warm solution, in a suitable flask protected by a reflux condenser, was treated gradually with solid sodium nitrite. The mixture was next heated to boiling, then allowed to stand in a warm place for several hours, after which the product was isolated in a suitable way.

*Contribution from the Laboratory of Organic Chemistry of the State University of Iowa.

For treatment with hypophosphorous acid the base was converted into the hydrochloric or sulfuric acid salt, the solution cooled to about 0 degrees and diazotized with sodium nitrite solution according to the standard method. To the resulting liquid there was added 10 per cent. excess of a 10 per cent. solution of hypophosphorous acid and the mixture allowed to stand for four days in the ice chest at a temperature not above 5 degrees, after which the product was isolated and purified. The yields are given in Table I.

TABLE I

DECOMPOSITION OF DIAZONIUM SALTS

Amino compound	Product	Yields with different reagents	
		Alcohol	Hypophosphorous Acid
Aniline	Benzene	[a]	60
p-Toluidine [b]	Toluene	40	67
β-Naphthylamine	Naphthalene	7 [c]	13
2,4-Dichloroaniline	1,3-Dichlorobenzene	45 [c]	50
2,4-Dibromoaniline	1,3-Dibromobenzene	—	73
2,5-Dibromoaniline	1,4-Dibromobenzene	—	69
2,6-Dibromoaniline	1,3-Dibromobenzene	—	49
sym-Tribromoaniline	1,3,5-Tribromobenzene	72 [d]	70 [d]
2-Amino-5-bromotoluene	3-Bromotoluene	52 [e]	—
3-Bromo-4-aminotoluene	3-Bromotoluene	60	—
3-Amino-6-bromotoluene	2-Bromotoluene	—	79
3-Amino-4,6-dibromotoluene	2,4-Dibromotoluene	—	65
3-Amino-2,4,6-tribromotoluene	2,4,6-Tribromotoluene	—	91
3-Amino-6-bromobenzoic acid	2-Bromobenzoic acid	34 [f]	75
2-Amino-5-bromobenzoic acid	3-Bromobenzoic acid	32 [f]	—

a. Under the conditions alcohol gave unsatisfactory results. Sodium stannite gave a 60% yield of benzene.

b. With alcohol *o*-tolyldiazonium salt gave a 45% yield of *o*-tolyl ethyl ether. Treatment with hypophosphorous acid gave some *o*-cresol, and much tar, but no toluene. Treatment of the *m*-tolyl salt with hyphophosphorous acid gave a small portion of *m*-cresol, much tar, and no toluene. Repeated tests gave the same results.

c. The alcoholic solution of the amine salt was diazotised by treatment with isoamyl nitrite in presence of sulfuric acid. After standing for several hours at room temperature the mixture was heated to boiling under reflux for a short time.

d. These figures represent purified material. The yields of crude products were 91 and 94%, respectively.

e. Remsen and Orndorff's method [*Am. Chem. Jour.*, 9, 387 (1887)] modified by Coleman and Talbot [*Org. Synth.*, 13, 96 (1933)] was used.

f. The diazonium salt was prepared as directed by Cameron [*Am. Chem. J.*, 20, 229 (1898)].

Summary

Amines containing various substituents in different positions with respect to the amino group have been diazotized, and the resulting diazonium salts have been treated with alcohol and hypophosphorous acid, respectively. In cases where a given amine gave a product with both reagents, the highest yield was obtained with hypophosphorous acid.

Iowa City, Iowa.

REFERENCES

1. Griess: *Ann.*, **137**, 68 (1866).
2. Fischer and Fischer: *Ann.*, **194**, 270 (1878).
3. Wroblevsky: *Ber.*, **3**, 98 (1870); *Ann.*, **168**, 210 (1873).
4. Remsen and Orndorff: *Am. Chem. J.*, **9**, 397 (1887).
5. The effect of ortho substituents in the acceleration of other reactions has been noted by Raiford, Taft and Lankelma. [*J. Am. Chem. Soc.*, **46**, 2051 (1924).]
6. Jackson and Moore: *Am. Chem. J.*, **12**, 167 (1890).
7. Cameron: *Am. Chem. J.*, **20**, 251 (1898).
8. Mai: *Ber.*, **35**, 162 (1902).

Mystery of Fatal Blood Disease Now Nears Solution

The mystery of agranulocytosis, new and fatal disease of too few white cells in the blood, seems nearer solution as a result of studies reported by Drs. Francis P. Parker and Roy R. Kracke of Emory University, Ga., to the American Society of Clinical Pathologists.

The disease is apparently caused by certain of the popular and largely prescribed coal tar derivatives, particularly those derived from benzene. That discovery, however, did not entirely solve the mystery of the disease because so many persons use these drugs in large quantities while comparatively few develop the disease.

Benzene's effect of reducing the number of white blood cells may take place by reducing the amount of a sulfur-containing substance found in blood and bone marrow, the studies now reported indicate. This substance is glutathione and it is thought to be responsible for speeding up cell division in the bone marrow where blood cells are formed.

The disease is twice as common among women as men. First observed in 1922, it seems to have been on the increase in recent years. It caused thirteen hundred deaths in the United States during the three years 1931-1934. It starts suddenly with fever and sore throat and usually ends fatally in spite of vigorous treatment.

BIOPHOTOGENESIS AND CHEMILUMINESCENCE*

By J. Howard Graham

"TO HIM who in the love of nature holds communion with her visible forms, she speaks a various language." The visible forms which we will consider are those made visible by the light they emit. On a hot summer night when the air is still, it needs only a casual observer to notice the myriads of light scintillations over and through the bushes and grass; and if he peers through the grass to the ground, he may notice the slow motion of glow worms, which are, in most cases, the larvæ of the firefly. Perhaps it is a walk through a dark, moist woods, when close observation will reveal glowing fungi and decaying wood, while over marshes and stagnant pools, a fire, known as Ignis fatuus (Will-o'-the-Wisp, Jack O'Lantern, spunkie) less well known, and appearing as a pale bluish flame, appears steadily or intermittently in spots. Ocean waters, viewed fore and aft from a steamer, seem full of glowing objects. Or it may be that a tourist during a typical tropical night, may venture to row on the quiet waters of a harbor such as Santiago, Cuba, when, as he dips his oar down into the inky depths, its full length is made apparent by a soft glow and the retrieved oar drips brilliant liquid drops. Along the hilly shore, the Cuculles beetle, Pyrophorus noctilicus, wings its slow rectilinear flight as though it were a lantern in the hand of an approaching visitor. Its light is so intense that it has always attracted the attention of tourists. Native boys on the street sell cages of three and four beetles, the light of which is sufficient to read newsprint. So attractive to the tourists are these beetles, that the many attempts to bring them north have resulted only in a shortened life of the insect.

Biophotogenesis is a term applied to the development of light by life processes. While the phenomenon is very common, adequate explanation is yet to be discovered. Physicists call it "cold light," and it is their dream to attain its brilliancy and economy by artificial means. Some think it is induced by true chemical reactions; but attempts to reproduce it by true chemical reactions apart from life processes, result in the phenomena of chemiluminescence. Glowing was thought by early investigators to be due to the element phosphorus or its compound phosphine; but today this is known not to be true.

*Read at the 1935 Meeting Pennsylvania State Pharmaceutical Association, June, 1935.

A recent survey (1) disclosed the fact that there are at least thirty-six orders of animals, containing one or more forms known to produce light, while the plant kingdom has very few forms with autogenous light production. Among the latter are some bacteria and some fungi, the light production of which can be traced through the threads of mycelium which penetrates decaying roots and stumps. (2, 12)

Biophotogenesis has been studied by several observers and mostly with animals. The following are those most prominently mentioned in the literature: Cypridina hilgendorfii, (3, 4) a marine crustacean of the order Ostracoda; the Coleoptera representatives are the beetles Photinus pyralis. Photinus castus, (5) Photurus pennsylvanicus (6, 9) and Pyrophorus noctilicus; (7) among the molluscs, Pholada dactyle, (8) a rock-perforating animal of the class Schapopoda. Others have studied the luminous bacteria of the swordfish (10) and fungi such as Agaricus melleus (4) popularly called fox-fire. The various phases of study have included the light-producing organs; the light-producing habits of the individual; the spectral energy distribution of the emitted light; comparisons of the animal light with our own common artificial light sources, and even the separation and crystallization of one of the active principles called "luciferin." (14)

The history of the development of our knowledge along these lines is interesting. Aristotle is said to be the first one to record his observations on the luminosity of dead fish and domestic animals. Such articles written up until the last century did not mention the fact that light emanates from living organisms or tissues. Robert Boyle in 1667 took a piece of glowing decayed wood, placed it under the receiver of an air pump, thus exhausting the air, and he noticed a marked diminution in the glowing, thus proving the necessity for air in the production of the luminescence. In 1794, Spallanzi moistened some dried material that had been luminous in life and it glowed under the moistening process. This proved that water was needed. In 1887, DuBois made the discovery that two other materials besides oxygen and water are needed. He gave them names, as we shall see. So it is now a fact, generally accepted, that oxygen, water, and two (at least) biochemically produced substances are needed for the glowing of most, if not all, of the creatures studied so far. In 1810, McCartney set forth his views regarding the luminiscence of the sea. He believed it to be caused by the living things in it. (11) During the years 1915-16 there was a series of lectures given at the Franklin Institute by Professor

Ulric Dahlgren (12) of Princeton University, and these lectures will stand out as a monument to his extensive biological experimentation and collaboration. Therein is his reminder that plant and animal life arose out of the crystallizing cosmos of our planet Earth, and that the living forms were endowed with the ability to maintain their existence and at the same time replenish worn-out material with new, while all the time emitting energy, which with some animals like the dog, horse and squid, takes the form of motion; with the bee and the bird, it is heat; with some water creatures like the Gymnotus or Torpedo it is electricity that is generated; with the fireflies, fish, worms, and some other lower forms of life, it is light. Dahlgren discusses at great length the luminous sponges (Porifera); jelly-fish (Coelenterata); sea-pens and sea-feathers (Pennatulidæ) brittle-stars (Echinoderms); squids (Cephalopods); worms (such as Sagitta); crustaceans (Ostracoda); bacteria (Bacillus pfluggeri and Microspira luminosa); and the plankton creatures such as Radiolaria. He says that of all the countries of the world, Australia's forests contain the most numerous and the brightest fungi.

The materials, two of them apparently necessary for the luminescent phenomena, are luciferin and luciferase. Kanda (13) describes the preparation of luciferin from Cypridina as follows: by drying the insects in direct sunlight, sifting out the shells, and extracting the body parts with absolute methyl alcohol. The extract is evaporated to a syrup on the water bath. To this syrup, ethyl alcohol is added in excess. Luciferin dissolves while certain impurities precipitate. The mixture is filtered, the filtrate evaporated almost to dryness, and the residue then taken up in water saturated with hydrogen. The solution is saturated with powdered ammonium sulphate which completely precipitates the luciferin. This precipitate is filtered and washed with saturated ammonium sulphate solution and the precipitate and filter paper dried over calcium chloride in a vacuum. The luciferin is extracted with absolute methyl alcohol giving a solution which is clear and fairly stable. It gives a brilliant light when luciferase is added. It gives no Millon or ninhydrin reaction but does give a positive Molish test. Luciferin prepared as above and in solution of water, is not precipitated by heavy metals, acids or alkalis.

Sayko Kanda (14) describes the preparation of crystalline luciferin by using Cadmium Chloride solution to precipitate from alcoholic solution the lecithin-like substances of Cypridina. The filtrate is freed

of alcohol and extracted with benzene and from the dried benzene extract, which produces a brilliant light with luciferase, luciferin crystals can be obtained by using ether or benzene.

Luciferase is obtained by treating with water material which has been previously extracted by organic solvents such as alcohol. Luciferin is soluble in alcohol; luciferase is not. Both are soluble, however, in water. Luciferin is probably a new natural proteose, soluble in alcohol, dialyzable, and not digested by trypsin. Luciferase is probably an albumin and as such is not soluble in alcohol, is non-dialyzable, and is classed as an enzyme. (15)

Whole dried Cypridina contain iron, copper and manganese, and while such is the case, it is not certain that these are concerned in the action of luciferase. The latter appears to be an organic catalyzer which accelerates the oxidation of the luciferin, the intensity of the luminescence being dependent upon the reaction velocity or rate of oxidation. By mixing luciferin of one species of firefly with the luciferase of another species, Harvey was able to show that the light produced is characteristic of the animal supplying the luciferase. (1)

DuBois (16) represents the various phases of biophotogenesis and the natural synthesis of luciferin as follows:

(1) Coluciferase plus preluciferin = luciferin
(2) Luciferase plus luciferin = oxyluciferin
(3) Oxyluciferin plus oxygen = light

Harvey (1) does not agree with this and offers his explanation as follows:

(1) Luciferin plus oxygen = oxyluciferin plus water
(2) Luciferin H_2 plus oxygen = luciferin plus water (a sort of leuco form)
(3) Luciferin H_2 plus luciferase plus oxygen = luciferin plus luciferase plus luminescence.

With high pressure oxygen, the reactions proceed to the right; with low pressure oxygen, to the left. There is light production only in the presence of luciferase.

The Light Organs

With many of the luminous creatures there is a lens-like eye, for directing the light where wanted. There is also a layer of cells which contain a shiny material and this makes the layer act as a reflector so that when light is produced in the middle of the organ, all is shot out and through the lens in a concentrated beam. The organs of the creature are protected from this light they produce, by some sort of screen. The firefly has no true lens, the light merely shining through the cuticle which is transparent over the light organ, whereas over the rest of the body it is dark and pigmented. One species has at least three colored luminous organs: blue, violet, and reddish. The tracheal end-cell is responsible for the control of luminescence, control being effected by the regulation of the oxygen supply entering the photogenic cell. (17)

Physical Nature of the Light

The nature of the light from various creatures has been examined carefully. Each creature has its own type of illumination such as to intensity, flashing time, color or hue, spectral features, etc. The efficiency of chemiluminescent reactions is scarcely more than one per cent. that of bioluminescent reactions. The efficiency of the firefly is 100 per cent. in so far as light within the visible spectrum is concerned; and the amount of heat emitted is so small that the possibility of measuring it exactly is doubtful. Attempts to this purpose have been made. No artificial illumination has at the most more than 4 per cent. efficiency compared with that of the firefly. However, this light is not 100 per cent. efficient when the color spectrum is taken into consideration. It would be most trying as artificial illumination since most objects have a consistently greenish hue. Bioluminescence is the cheapest light we know. It is the "cold light" of the physicist, and we are not aware that we will ever be able to produce it efficiently. However, a study of these wonderful phenomena of nature appeals to the intellect and in this role has attracted dozens of investigators. By a greater co-operation of the research students of Biology, Physics, and Chemistry, our knowledge of luminescence promises to be greatly extended.

It takes a great deal of curiosity and even some courage to betake oneself beyond the confines of cozy rooms and into the dark damp

places where glowing creatures exist, and furthermore it takes skill to catch the creatures that are definitely responsible for the glowing. Just why they glow we do not know. It is believed by some that the eyes of cats and dogs glow. This is not true, for no eye is known which gives out light of its own. The light of a cat's eye is reflected. As to the squid and shrimp and other sea animals, some believe that they use their light as lanterns; but this explanation cannot hold, for the creatures that live at great depths are blind. It is difficult to explain their light. With others, it may be that predaceous creatures are warned off by the sudden glowing of possible victims. Where ejected secretions glow, these are probably used to bewilder the pursuer. The sea-pen or sea-feather may glow in order to attract small organisms upon which to feed, and light such as that of the firefly may be used for identification purposes, for play, or as a signal to attract for mating purposes.

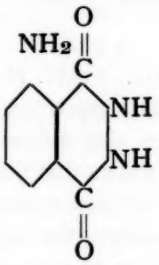
Chemiluminescence

This name implies the production of light during chemical reactions at low temperatures. They are oxidation reactions involving the absorption of gaseous or dissolved oxygen, and this is a distinguishing criterion. The glow of phosphorus was what first attracted Brandt in 1669 to the discovery of this element. Sodium and potassium when freshly cut and at 70 degrees C. will glow for some time. Ozone makes some organic substances glow, and pyrogallol is especially bright under certain conditions. About fifty different substances, principally organic, are named as glowing under proper conditions. (1)

Spectra taken of luminous animals are quite similar to those of chemiluminescent reactions and both require oxygen for light production. The light of luminous animals is due to some material produced in their cells, and when we are able to write the chemical formula of this photogenic substance and tell exactly how the oxidation proceeds, the problem of light production in animals will be solved.

Within the past year, a new organic chemical has been synthesized and found upon mild oxidation with potassium ferricyanide and hydrogen peroxide in the presence of sodium hydroxide to glow brighter than any previously prepared artificial or natural substance. It is far superior to luciferin in this respect. The originators (18) call it

"luminol" because of its light-giving properties and the enolic nature of its chemical constitution. It is 3-amino phthalhydrazide, and is an exceedingly interesting substance.



BIBLIOGRAPHY

1. Harvey, E. N.: "The Nature of Animal Light," Book. J. B. Lippincott Company (1920).

2. Mangold: *Handb. der Vergleich Physiologie* 3 (1911).

3. Harvey, E. N.: *J. Gen. Physiol.* 1, 269-93 (1919).

4. Colblentz and Hughes: *Bur. Std. Papers* 21, 521 (1926).

5. McDermott, F. A.: *J. A. C. S.* 37, 401-4 (1915); 37, 396-401 (1915).

6. Lutz, F. E.: "Field Book of Insects."

7. Author.

8. DuBois, R.: *Compt. rend.* 166, 578-80; *Compt. rend. Soc. Biol.*, Dec. 22, 1917.

9. Snell, P. A.: *J. Cellular Comp. Physiol.* 1, 37-51 (1932).

10. Hayasi, K., and Okuyania, M.: *Chem. Zentr.* 1630 (1931).

11. Harvey, E. N.: *Scientia* 41, 343-54 (May, 1927).

12. Dahlgren, U.: *J. Frank. Inst.* 180, 515, 711 (1915); 181, 243, 377, 525, 659, 805 (1916).

13. Kanda, K.: *Amer. J. Physiol.* 68, 435-43 (1924).

14. Kanda, S.: *Sci. Papers Inst. Phys.-Chem. Research* (Tokyo) 18, 1 (1932).

15. Harvey, E. N.: *J. Gen. Physiol.* 1, 269-93 (1919).

16. DuBois, R.: *Comp. rend. Soc. Biol.* 81, 317-19 (1918).

17. Snell, P. A.: *J. Cellular Comp. Physiol.* 1, 37-51 (1932).

18. Huntress, Stanley and Parker: *J. Chem. Ed.* 11, 142-145 (1934); Harvey, E. N.: *Science* 40, 33-34 (1914); Stephens, K. P.: *J. Gen. Physiol.* 10, 859-73 (1927); Harvey, E. N.: *J. Gen. Physiol.* 10, 875-81 (1927); Adams, E. Q.: *Bull. Natl. Research Coun.* 59, 30-40 (1927); Harvey, E. N., and Snell, P. A.: *Proc.. Am. Phil. Soc.* 69, 303-8 (1930); Anderson, R. S.: *J. Cellular Comp. Physiol.* 3, 45-59 (1933).

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Arthur Osol, Ph. D.

Hydrogen-Ion Concentration of Tears. G. N. Hosford and A. M. Hicks. *Archives of Ophthalmology,* January, 1935. The authors present a synopsis of previous work on the determination of the hydrogen-ion concentration of tears. It is shown that the tears are sufficiently buffered to permit the degree of dilution necessary to render the determination of the hydrogen-ion concentration easily applicable to clinical cases. The average hydrogen-ion concentration of tears from healthy eyes which were free from symptoms closely approximates the pH of blood, namely, 7.35. Lipschutz' observation that "the sensations experienced by a patient when solutions are dropped into the conjunctival sac or on the cornea are much more intimately related to the pH of the solution than to its osmotic pressure" is confirmed, and success in the relief of some conjunctival and corneal symptoms by the modification of the pH of the tears by the instillation of appropriate buffer solutions is described. The relation of the pH of the tears to certain bacteria and to the healing of conjunctival and corneal lesions is discussed. (Through *Chemist and Druggist, 122,* 400, 1935.)

Buffer Solutions in Ophthalmology. S. R. Gifford. *Archives of Ophthalmology,* January, 1935. The author recommends the use of the following stock solutions for the preparation of buffer solutions suitable for ophthalmologic use:

(1)	Boric Acid	12.4 Gm.
	Potassium Chloride (anhydrous)	7.4 Gm.
	Distilled Water	1000 cc.
(2)	Sodium Carbonate (anhydrous)	21.2 Gm.
	Distilled Water	1000 cc.

The reactions obtained by adding varying amounts of the stock sodium carbonate solution to 30 cc. of the boric acid solution are as follows:

Sodium Carbonate Solution	Reaction
cc.	pH
0	5.0
0.05	6.0
0.10	6.2
0.25	6.75
0.50	6.95
1.00	7.2
1.50	7.6
2.00	7.8
3.00	8.2
4.00	8.4
8.00	9.0

For phenacaine and butyn the acid buffer solution No. 1 (pH 5.0) is suitable; for zinc salts this solution is practical, but a less irritating solution is pH 6.0. Most alkaloids are best absorbed, as well as less irritating, in a slightly alkaline solution of pH 7.6. In vernal conjunctivitis and certain cases of chronic conjunctivitis with tenacious secretion a solution of pH 8.4 is suitable. A solution of pH 9.0 is only used to dissolve sodium fluorescein. (Through *Chemist and Druggist, 122,* 401, 1935.)

Liquid Extract of Liver. The first supplement to the Dutch Pharmacopœia (fifth edition) describes the following process for the preparation of liquid extract of liver: Macerate for twelve hours, with frequent agitation, 10 kilos of fresh ox liver, previously passed through a mincing machine with apertures of 3 mm., with a mixture of 15 liters of water and 20 cc. of dilute hydrochloric acid (41 per cent.). Heat to 80 degrees, strain and press. Evaporate the liquid on a water bath to 1 kilo and when cool add to the residue 1500 cc. of alcohol (95 per cent.). Shake the liquid for ten minutes, filter, remove the alcohol by distillation and evaporate the residue to 300 cc. Mix the product with 3000 cc. of alcohol (95 per cent.), shake for ten minutes, then set aside for twelve hours, at the end of which time pour off the spirituous liquid and dissolve the residue in water to pro-

duce a volume of 1350 cc. Finally add 150 cc. of spirit of cinnamon. A clear, dark brown, very slightly acid liquid, of which 15 cc. is equivalent to 100 grams of liver. (Through *Chemist and Druggist, 122,* 396, 1935.)

Studies in Injection Medicine. I. The Decomposition of Cocaine Solutions on Sterilization and Standing. S. A. Schou and E. Heim. *Pharm. Acta Helvetica, 10,* 31 (1935). The authors describe a method for determining the degree of hydrolysis of cocaine solutions. It is found that cocaine solutions require no addition of buffer for the latter accelerates hydrolysis to such a degree that the solutions become useless. Pure aqueous solutions of cocaine hydrochloride can be sterilized in a current of steam at 100 derees C. for 30 minutes without hydrolysis if the solutions are stored in alkali-free glass. In the presence of a small amount of free hydrochloric acid (1 cc. of 0.1 normal hydrochloric acid per 100 cc. of solution) solutions can be sterilized by autoclaving at 120 degrees for 20 minutes without hydrolysis.

Studies in Injection Medicine. II. Decomposition of Novocaine Solutions on Sterilization and Standing. J. Abildgaard. *Pharm. Acta Helvetica, 10,* 38 (1935). The details of the method for determining the degree of hydrolysis of procaine solutions are given. It is reported that procaine in 0.001 normal hydrochloric acid solution is stable when sterilized in a current of steam, the extent of hydrolysis being no more than 2 per cent. The hydrogen-ion concentration of the solution is not affected by sterilization. Aqueous solutions which do not contain hydrochloric acid or a buffer may be sterilized in a current of steam, but upon autoclaving about 5 per cent. of the procaine is destroyed.

A Reaction for Distinguishing Quinine from Quinidine. L. Rossi and J. A. Sozzi. *Quim. e. ind., 11,* 199 (1934). Through *Chem. Abstracts, 29,* 2305 (1935). Quinine and quinidine are optical isomers

and most of their chemical reactions are identical. Thirty commonly used alkaloidal reagents are listed which give the same tests with both. To a solution of the pure alkaloid in very dilute sulphuric acid add a drop of $KI.I_2$ solution, shake and dilute, if the precipitate is heavy, until a light translucent suspension is obtained. The quinine precipitate appears dark drown, the quinidine precipitate yellow.

Tetraamino Cupric Sulfate. II. Pharmaceutical Data. E. del Carlo and P. G. Paternosto. *Rev. facultad cienc. quim.* (Univ. La Plata) *9*, 41 (1934). Through *Chem. Abstracts, 29*, 3459 (1935). Aqueous solutions of tetraamino cupric sulfate are stabilized by the addition of 10 per cent. sucrose or glycerol and are used for intravenous injection in streptococcic infections. Addition of ammonium benzoate or of Seignette salt allows sterilization by heat.

A New Semi-Microdetermination of Organically Combined Halogens by Titrimetric Means. W. Kimura. *Fettchem. Umschau, 42*, 32, 41 (1935). Through *Squibb Abstract Bulletin, 8*, 583 (1935). The method is based on Stepanow's reaction employing sodium and ethyl alcohol and titrating the halogens split off by Volhard's method (*Ber., 39*, 4056, 1906), except that normal butyl or benzyl alcohol is used in place of ethyl alcohol. The procedure is as follows: 0.02 to 0.05 gram of substance is weighed into a micro-dish 12 mm. in width and 5 mm. in height and the dish placed in a reduction flask. After addition of 3 cc. of normal butyl or benzyl alcohol, the reflux condenser is attached and the substance dissolved by gentle heating. 0.2 gram of freshly cut sodium (0.2 to 0.3 gram in the case of benzyl alcohol) is introduced through the condenser into the flask, carefully heated with shaking, and then rapidly boiled for 20 to 30 minutes. After cooling, the contents of the flask are dissolved in 30 to 50 cc. of water and acidified, while cooling, with 5 cc. of cold nitric acid. After the addition of 5 cc. of ether and 10 cc. of 0.05 normal silver nitrate, the flask is vigorously shaken until the liquid is clear and then the solution is titrated with 0.05 normal ammonium thiocyanate. The indicator is 40 per cent. ferric ammonium sulfate solution (1 to 2 cc.). Blank tests are made in the same way.

When working with an iodide, the contents of the flask and the nitric acid for acidification are cooled with ice. The excess of nitric acid must be such that the solution is just acid to litmus. It is still better in the case of bromine and iodine derivatives to add the silver nitrate before the nitric acid. With stable halogen derivatives larger amounts of alcohol and sodium are used and the substance boiled for a longer period of time.

The Use of Propylene Glycol as a Solvent. John Rae. *Pharm. Jour., 134,* 590 (1935). Some experimental work on the use of ethylene glycol as a solvent, particularly of vegetable coloring matter, has already been recorded. (*Quart. Jour. Pharm. Pharmacol., 6,* 483, 1933.) The toxicity of this solvent, taken in large doses, would appear, however, to be more or less established; and it is probably not desirable to use it in any preparations which might be used internally. On the other hand, propylene glycol would appear to be quite free from any toxic properties. (*J. Pharmacol. and Exper. Ther., 44,* 109, 1932.)

Accordingly the author carried out experiments to determine the solvent power of propylene glycol on cochineal, cudbear, aloes and catechu. From these experiments it appears that propylene glycol is not as good a solvent as ethylene glycol of defatted cochineal, but in the case of cudbear it is superior. Propylene glycol is a solvent of the constituents of aloes which react with ammonia, and of tannins in catechu. All of the solutions prepared have remained quite bright and free from deposit for a period of three months. It is suggested that further work should be done to test the non-toxic properties accredited to propylene glycol; and to confirm the toxicity of ethylene glycol, as both these solvents should prove of great use in pharmaceutical preparations if they can be used with safety.

Dispensing Notes From Abroad

Aspirin and Potassium Citrate. The querist would like to know whether or not the following prescription will form a clear mixture upon compounding the ingredients.

Acetylsalicylic Acid	3 drachms
Potassium Citrate	4 drachms
Citrated Caffeine	2 drachms
Compound Tincture of Cardamon	2 fluidrachms
Water, to make	8 fluidounces

The mixture requires 2 additional drachms of potassium citrate to make clear solution. Mix the acetylsalicylic acid and potassium citrate together in 5 fluidounces of water (1 drachm of acetylsalicylic acid will not dissolve). Dissolve the citrated caffeine in 2 fluidounces of warm distilled water, mix with the first solution, add the tincture and make up to 8 fluidounces with water. Affix a "shake-well" label. Of the insoluble drachm of acetylsalicylic acid, about 11 grains will dissolve in the 8 ounces of water, and an additional small quantity may be dissolved in the diluted tincture. The remainder will not form an unsightly mixture, so need not be suspended with gum or mucilage. Many dispensers prefer, however, to add 1 drachm of compound powder of tragacanth to ensure a uniform mixture. (*Chemist and Druggist.*)

Quinine Sulphate and Sodium Salicylate. Directions are requested for compounding the following ingredients:

Quinine Sulphate	6 grains
Sodium Salicylate	2 drachms
Linctus Gee	2 fluidounces
Compound Powder of Tragacanth	q. s.
Peppermint Water, to make	6 fluidounces

Quinine salicylate is precipated as a sticky resinous mass. This difficulty may be overcome by preventing the quinine salicylate particles from agglomerating by means of the mucilage. The following is the correct procedure for compounding the ingredients: Reduce the quinine sulphate to fine powder and mix with 60 grains of compound powder of tragacanth. Gradually add a little peppermint water, triturate to a smooth cream, then add the linctus. Dissolve the sodium salicylate in 3 fluidounces of peppermint water, add to the quinine suspension and make up to volume. The precipitate which is produced is readily diffused on shaking. (*Pharm. Jour.*)

Phenobarbitone (Phenobarbital) in Mixture. The white crystalline deposit which developed on standing in the following mixture:

Chloral Hydrate	15 grains
Sodium Bromide	15 grains
Soluble Phenobarbitone	1½ grains
Peppermint Water, to make	½ fluidounce

was found, by elimination, to be due to the reaction between chloral hydrate and the soluble phenobarbitone. It consists of phenobarbitone base, and its formation appears to be due to the interaction of the alkali of the sodium derivative with the chloral hydrate. The best method of dispensing the prescription would be to replace the soluble phenobarbitone with an equivalent weight of phenobarbitone, using mucilage of tragacanth as a suspending agent. (*Pharm. Jour.*)

Nux Vomica and Ammonia. The development of a blue color in mixtures containing galenical preparations of nux vomica with aromatic spirit of ammonia has been known for many years. It was reported upon in 1900 by Mr. Rutherford Hill, who suggested that it was due to the presence of copper. In 1924 Mr. F. G. Hobart contributed a paper on the subject showing that there was not sufficient copper to account for the color, and suggested that the cause was the presence of caffeo-tannic acid, since other drugs containing this constituent also gave the same color.

Sodium Bicarbonate and Magnesia. The following ingredients are reported to have produced a mixture which becomes strongly alkaline with a decided soapy taste.

Potassium Citrate	2 drachms
Magnesia	1½ drachms
Sodium Bicarbonate	2 drachms
Chloroform Water, to make	6 fluidounces

The explanation is offered that magnesia and sodium bicarbonate react with the formation of magnesium carbonate and sodium hydroxide. Replacing the magnesia by magnesium carbonate will obviate this difficulty.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D.

When carbon crystallizes it does so in two sharply contrasting forms: the engaging diamond and the much less engaging graphite.

Graphite, a soft, easily led material, wherever it went left a trail of carbon in its wake, and hence found use in writing; hence, too, its name, for it comes from the Greek "graphein," to write.

When the strange plastic of Peru, caoutchouc, was introduced to merry England its first noted useful property was that of erasing graphite marks on paper, and it was accordingly dubbed "rubber," and rubber it has been ever since, though its uses have a hundredfold multiplied.

So do new words squirm into our dictionaries and so do they stay despite their inadequacy.

Vitamin products have spectacularly increased in use. From tenth to third place among pharmaceuticals in three years is their record of manufacture and sale. Today, so we are informed, only peristalsis persuaders, and cures (?) for colds exceed them in volume of business, and they bid fair to head the class if the curve of their sales continues to rise as it recently has. Research in their nature and application continues, and if we believe all we read, the millenium has come, the promised panacea our possession, and our dietary deficiencies done.

But casting aside the chaff, and coming to the real substance, even the most conservative will admit that the vitamin issue is an important one, in its present status and certainly in the possibilities that lie ahead.

Optochin (ethylhydrocupreine base) is an antiseptic chemical which has had some reputation as an enemy of the two-faced pneumonia germ. It has been also used as an eye lotion manifestly where the pneumococcus was the offending invader. Now, however, it comes into a new field of application. Heralded as an "antiseptic for cosmetic preparations," it offers certain definite advantages. It is an odorless white powder, insoluble in water (the salts are soluble) and soluble in alcohol, and similar to quinine in toxicity. For dandruff dissipators, antiseptic creams, and the like, we can foresee for it some degree of use, but its ministry should be most evident in the colored sticks and salves for lips, upon whose crimson platforms the lurking pneumococcus waits for osculation's transfer.

Bullets for bacteria is a new idea in the manufacture of vaccines and other suspensions of murdered germs.

This ingenious method of preparing vaccines or antigens for treatment of bacterial diseases has been developed at the University of California and is said to have certain advantages over the ordinary methods.

In common practice, vaccines are prepared by killing the disease bacteria in their cells by heat or chemicals or short wave radiations which, it is claimed, may result in an alteration in the protein of the bacteria. By the new method this undesirable reaction is eliminated. A type of ball mill has been perfected which consists of a cylinder containing several thousand steel ball bearings which kill the bacteria without denaturing the protein.

Effectiveness of this method has been demonstrated in the treatment of whooping cough and other ailments, according to the report.

It was the pharmacist, Waldie, of Liverpool, England, who suggested to the Scotch surgeon Simpson, that the heavy liquid called

chloroform might prove a good anæsthetic. Accepting the chemist's suggestion, Dr. Simpson first tried it on himself and his associates. The effects, at first intoxicating, so much so that bystanders charged the experimenting doctors with having imbibed too strongly of distillate of oats, eventually achieved to the customary complete anesthesia, and the experimenters dropped unconscious to the floor.

Announced to the profession, the discovery was not hailed with much enthusiasm. Simpson persisted, however, in his use of the drug, but it was not accepted generally until he administered it to Queen Victoria. He used it very cleverly only during certain spells of pain, and did not apply enough to cause a complete narcosis. This form of application was accordingly called "Narcosis à la Reine," a name which is still used in European medical journals.

The maggot treatment of sores is not pleasant in theory or in practice, and the sight of an ulcer of the leg squirming with spectral worms that burrow to the very bones is not a safe pro- or post-prandial exercise. But indolent sores *do* yield to maggot magic.

And here is how *Science* explains it:

Dr. William Robinson, of the Bureau of Entomology and Plant Quarantine, now finds that allantoin, which is given off by maggots as they work their way through a wound, is responsible for part of their healing power. Allantoin, Dr. Robinson says, is not a new discovery. Dr. C. J. Macalister, who used it successfully twenty-three years ago for ulcers, reported that European peasants had long applied the roots of comfrey, which contain allantoin, to sores.

His recent tests, Dr. Robinson says, show that allantoin is particularly use for non-healing wounds, such as chronic ulcers and extensive burns that refuse to mend. After a few treatments, pinkish granulation tissue begins to grow and soon the tissues are knitting to-

gether rapidly. A specially promising feature of the new treatment is that it can be made to control healing. Healing from the bottom up can be insured in a deep wound by applying the allantoin solution in a small packing at the base of the wound and covering the sides with vaseline. General granulation can be promoted by filling the wound with gauze well saturated with the solution.

According to a recent article appearing in Drug and Cosmetic Industry, *deaths from reptile bites are in this country rapidly becoming rare, due mostly to the specificity of anti-venom serum.*

Between fifteen hundred and two thousand persons in the United States are bitten each year by poisonous snakes. As recently as ten years ago, about half of these bites were fatal, but today, thanks to a scientifically prepared serum, the death rate from such bites has been reduced to two per cent.—probably the result of improper or incomplete treatment.

The snake bite season in this country lasts from the end of April to the middle of October, except for those States around the Gulf of Mexico, where the season may extend throughout the winter months. The rattlesnakes, the copperhead and the moccasin are the only important poisonous snakes in the United States and one or more of these species are found in every State, with the possible exception of Maine and New Hampshire. Roughly speaking, over half the bites are from rattlesnakes, about 35 per cent. from copperheads, and about 10 per cent. from moccasins. Children are most frequently bitten, while farmers and other workers in rural disticts are also heavy sufferers. Fishers, hunters, campers, and vacationists are other groups frequently exposed, who are frequent victims during the year.

A sort of a symbiosis in business has just come to our ken. Canned flies and canned mushrooms, obviously offered in separate con-

tainers, are now in commercial production at one of our great mushroomeries. And this is how it happened, according to Dr. Little's "Industrial Bulletin":

Raising mushrooms calls for a heavy application of manure. This practice results in the hatching out of vast numbers of flies which are extremely difficult to get rid of.

An engineer recommended the installation of a suction fan which passed both air and flies over some refrigerating coils in such manner as to chill the flies and then drop them in a dormant state into large milk cans. The installation was made and the flies eliminated as a nuisance.

The canned flies are now shipped to frog raisers. Upon receipt the cans are immersed in a brine solution, which chills the flies and again renders them dormant. In that condition they are fed to the frogs.

The mushroom grower now realizes from the sale of flies nearly as much as from the sale of mushrooms.

And we've known open-air lunch counters where a similar device might operate with profit and at the same time change what seems like raisin pie to its pristine apple status.

The only accomplishment according to the same writer, which may seem worthy to rank with the foregoing was that of Professor Elihu Thomson in luring millions of male mosquitoes from the Lynn marshes to their destruction on the walls of an electric furnace by causing the furnace to emit a hum identical in pitch with that of the female mosquito.

Which suggests the calamitous position of a New Jersey snorer on a warm midsummer night, whose guttural reverbations happen to coincide with the pitch of Mrs. Mosquito's hum.

Speed has stolen most of distance's alleged enchantment and invention is rapidly fusing the peoples of earth. Soon the world be-

comes one country—and pioneering man must seek adventure in realms beyond his own. An Isabella inspired Columbus will more than likely find the moon in 2492—and week end excursions to Lunatic Land compete with Coney Island.

But finding a way to the moon will not be much of an achievement for there will still be left a million times ten million moons for mere man to find.

For instance there is I. C. 342, just reported by Shapley of Harvard—a mere speck in the roof of "my Father's House," and which in reality is a gigantic spiral nebula, or island universe somewhat like the one to which our little earth belongs.

And it is scarcely six trillion miles away—only a footstep in the measureless trail of the Unknown Overseer—whose eye is on the lily —and whose hand holds all of Heaven.

Hail the end of halitosis!—and the beginning of better friendships—for "your best friend *can* now tell you!!" A lasting remedy for offensive breath odors seems at hand.

Even the long lasting garlic loses its license to offend.

"The breath can be immediately and completely rid of the odor (garlic) by washing the teeth and tongue and rinsing the mouth with a solution of chloramine-T. The chlorine liberated in the mouth reacts chemically with the essential oils and deodorizes them. It is probable that many cases of foul breath from other causes would be amenable to the same method of treatment." This is according to Yale researchers working on this specific problem.

The solution of chloramine-T was made by dissolving one 4.6 grain tablet in a small amount of water. Chloramine-T is the well-known organic chlorine compound available at prescription pharmacies and is used in the treatment of wounds and for sterilizing drinking water.

In their experiments Drs. Haggard and Greenberg of Yale first proved that the source of most obnoxious breath is not systemic but local. It arises, at least in the case of onions and garlic, solely from particles retained in and about the structures of the mouth. Air in the lungs does not taint the blood; the stomach is not at fault, nor is the saliva.

1935 Status of Endocrine Research

I. Predemonstration Phase	
(a) Pineal	
II. Demonstration Phase	
(a) Thymus	
(b) Intestinal Tract:	(1) Cholecystokinin (2) Duodenal hormone
(c) Anterior Pituitary:	Adrenalotropic, Fat-metabolizing, Pancreatropic, Parathyreotropic, and Diabetogenic principles have been claimed.
III. Concentration Phase	
(a) Parathyroid	
(b) Anterior Pituitary:	(1) Gonadotropic, (2) Thyreotropic, (3) Lactogenic, and (4) Growth-promoting hormones.
(c) Suprarenal Cortex*	
IV. Isolation and Analysis Phase	
(a) Pancreas (Insulin)	
(b) Intestinal Tract (Secretin)	
(c) Posterior Pituitary:	(1) Alpha-hypophamine (2) Beta-hypophamine
(d) Ovary	(Theelin and related principles).
(e) Testis*	
V. Synthetic Phase	
(a) Corpus Luteum (Progestin)	
(b) Thyroid (Thyroxin, a derived principle)	
(c) Suprarenal Medulla (Adrenalin or Epinephrine)	

—(*From Therapeutic Notes.*)

*These two glands may be placed in Groups IV and V, respectively, if recent preliminary reports are confirmed.

A New Treatment for Narcotic Addiction

A new method of treating narcotic drug addiction which cured 31 out of 57 addicts was reported by Drs. Theophil Klingman and William H. Everts of Ann Arbor, Mich., to the meeting of the American and Canadian Medical Associations.

Hyoscine, one of the solanaceous alkaloids, and pilocarpine, the alkaloid from jaborandi, were the medicines used. Both of these have been tried before in treating drug addicts, Drs. Klingman and Everts pointed out, but they have modified the method of giving these remedies and believe they have developed a rapid, simple, painless and non-hazardous way to give relief from the craving for narcotics.

Hyoscine is given at the beginning of the six to eight weeks' treatment. This causes a mild delirium and has the peculiar effect of washing out of the mind all memory of events during the treatment. Hyoscine also tends to allay pain. Following this, pilocarpine is given. This quickly dispels the delirium. Further treatment consists in investigating the patient's mental state and environment and in making every possible adjustment.

Of the group of 57 so treated, 31 are now known to be free of the narcotic drug habit three and one-half years after the treatment. Seven relapsed after being free for from three to ten months. The other 19 could not be located to learn the results of the treatment.—(*Science News.*)